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EXAMINER

STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/821,689

Applicant(s)

WILLIAMS, JOHN G.K.

Examiner

Teresa E. Strzelecka

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-46 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-28, drawn to a polymerase-nucleic acid complex, said polymerase-nucleic acid complex comprising:

a target nucleic acid and a nucleic acid polymerase, wherein said polymerase has an attachment complex comprising at least one anchor, which said at least one anchor irreversibly associates said target nucleic acid with said polymerase to increase the processivity index, classified in class 530, subclass 812, for example.
 - II. Claims 29-46, drawn to a method for detecting incorporation of at least one NTP into a single primer nucleic acid molecule, said method comprising:
 - i. immobilizing onto a support a polymerase nucleic acid complex comprising a target nucleic acid, a primer nucleic acid which complements a region of the target nucleic acid, and at least one nucleic acid polymerase;
 - ii. contacting said immobilized complex with at least one type of labeled nucleotide triphosphate (NTP), wherein each NTP is labeled with a detectable label, and,
2. iii. detecting the incorporation of said at least one type of labeled NTP into a single molecule of said primer, while said at least one type of labeled NTP is in contact with said immobilized complex, by detecting the label of the NTP while said at least one type of labeled NTP is in contact with said polymerase nucleic acid complex, classified in class 435, subclass 91.2, for example.
3. The inventions are distinct, each from the other because of the following reasons:
4. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as

claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the method of Group II can be performed using an entirely different product, such as a polymerase attached to a microbead, rather than a product of Group I.

Searching the inventions of Groups I and II together would impose serious search burden. The inventions of Groups I and II have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for the polymerase-nucleic acid complex of Group I and the method of using immobilized polymerase are not coextensive, as the complex of claim 1 is not required to be immobilized on the support, while the polymerase of Group II is immobilized, but is not required to have the nucleic acid anchored to it. Therefore, prior art which teaches a complex of Group I would not necessarily be applicable to the method of detecting nucleotide incorporation of Group II.

5. Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

6. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Art Unit: 1637

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

7. This application contains claims directed to the following patentably distinct species:

Group I

Species of the attachment complex

- A) attachment complex comprises at least two anchors (claim 3),
- B) attachment complex comprises at least two anchors and is attached to a solid support (claim 4),
- C) attachment complex comprises a topological tether (claim 5),
- D) attachment complex comprises at least two anchors and a topological tether (claim 6),
- E) attachment complex comprises at least two anchors and a topological tether, and the

Art Unit: 1637

topological tether is attached to at least one anchor via a complementary binding pair (claim 7),

F) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least two anchor via at least two complementary binding pairs (claim 8),

G) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is a haptenic compound in combination with an antibody (claim 9, in part),

H) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is an haptenic compound in combination with a binding portion (claim 9, in part),

I) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is a haptenic compound in combination with an antibody fragment (claim 9, in part),

J) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is an antigenic compound in combination with an antibody (claim 9, in part),

K) attachment complex comprises at least two anchors and a topological tether, and the

Art Unit: 1637

topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is an antigenic compound in combination with an antibody binding portion (claim 9, in part),

L) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is an antigenic compound in combination with an antibody fragment (claim 9, in part),

M) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is a non-immunological binding pair (claim 9, in part),

N) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is receptor-receptor agonist (claim 9, in part),

O) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is receptor-receptor antagonist (claim 9, in part),

P) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is IgG-protein A (claim 9, in part),

Q) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is lectin-carbohydrate (claim 9, in part),

R) attachment complex comprises at least two anchors and a topological tether, and the

Art Unit: 1637

topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is enzyme-enzyme cofactor (claim 9, in part),

S) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is enzyme-enzyme inhibitor (claim 9, in part),

T) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is polynucleotide pair capable of forming nucleic acid duplex (claim 9, in part),

U) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is digoxigenin and anti-digoxigenin (claim 10, in part),

V) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is fluorescein and anti-fluorescein (claim 10, in part),

W) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is dinitrophenol and anti-dinitrophenol (claim 10, in part),

X) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is bromodeoxyuridine and anti-bromodeoxyuridine (claim 10, in part),

Y) attachment complex comprises at least two anchors and a topological tether, and the

Art Unit: 1637

topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is mouse immunoglobulin and goat anti- mouse immunoglobulin (claim 10, in part),

Z) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is biotin-avidin (claim 10, in part),

AA) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is biotin-streptavidin (claim 10, in part),

AB) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is thyroxine and cortisol (claim 10, in part),

AC) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is a phenylalanine derivative and hydrazine linker (claim 10, in part),

AD) attachment complex comprises at least two anchors and a topological tether, and the topological tether is attached to at least one anchor via a complementary binding pair, and the complementary binding pair is acetylcholine acetylcholine receptor (claim 10, in part),

AE) at least one anchor comprises at least one amino acid for attachment (claim 11, in part),

AF) at least one anchor comprises at least one epitope for attachment (claim 11, in part),

AG) at least one anchor comprises at least one amino acid for attachment and the amino acid is cysteine (claim 12, in part),

AH) at least one anchor comprises at least one amino acid for attachment and the amino acid is a phenylalanine derivative (claim 12, in part),

AI) at least one anchor comprises at least one amino acid for attachment and the amino acid is a histidine tag (claim 12 and 13, in part),

AJ) at least one anchor comprises at least one amino acid for attachment and the amino acid is a histidine patch (claim 12 and 13, in part),

AK) at least one anchor comprises at least one amino acid for attachment and the amino acid is a polyhistidine sequence (claim 12 and 13, in part),

AL) attachment complex comprises a topological tether and the tether comprises an antibody (claim 14),

AM) at least one anchor is attached to a solid support (claim 15),

AN) at least one anchor entraps target nucleic acid (claim 16),

AO) attachment complex comprises at least two anchors and a topological tether, wherein said topological tether is an antibody and said at least two anchors are each a histidine tag (claim 17).

Species of polymerases

AP) the polymerase is selected from family A polymerase (claim 20, in part),

AQ) the polymerase is selected from family B polymerase (claim 20, in part),

AR) the polymerase is selected from family A polymerase and is a Klenow polymerase (claim 21, in part),

AS) the polymerase is selected from family A polymerase and is a Taq polymerase (claim 21, in part),

Art Unit: 1637

AT) the polymerase is selected from family A polymerase and is a T7 polymerase (claim 21, in part),

AU) the polymerase is selected from family B polymerase and is a terminator polymerase (claim 22, in part),

AW) the polymerase is selected from family B polymerase and is a phi29 polymerase (claim 22, in part),

AX) the polymerase is selected from family B polymerase and is a RB-69 polymerase (claim 22, in part),

AY) the polymerase is selected from family B polymerase and is a T4 polymerase (claim 22, in part).

Species of polymerase complexes

AZ) the polymerase-nucleic acid complex is an array of polymerase-nucleic acid complexes attached to a support (claim 23),

BA) the polymerase-nucleic acid complex is an array of polymerase-nucleic acid complexes attached randomly to a support (claim 24),

BB) the polymerase-nucleic acid complex is an array of polymerase-nucleic acid complexes attached uniformly to a support (claim 25).

Species of processivity index

BC) the processivity index is at least 0.5 (claim 26),

BD) the processivity index is at least 0.8 (claim 27),

BE) the processivity index is 1 (claim 28).

Group II

Species of NTPs

- A) polymerase nucleic acid complex is contacted with a single type of labeled NTP (claim 30),
- B) polymerase nucleic acid complex is contacted with at least two different types of NTPS, and wherein each type of NTP is uniquely labeled (claim 31),
- C) polymerase nucleic acid complex is contacted with at least four different types of NTPS, and wherein each type of NTP is uniquely labeled (claim 32),
- D) NTPs are labeled on the γ -phosphate (claim 33),
- E) NTPs are labeled on the γ -phosphate with a fluorescent label (claim 34).

Species of detection of labeled NTP incorporation

- F) detecting using an optical reader (claim 35, in part),
- G) detecting using a high-efficiency photon detection system (claim 35, in part),
- H) detecting using a photodiode (claim 35, in part),
- I) detecting using a camera (claim 35, in part),
- J) detecting using a charge couple device (claim 35, in part),
- K) detecting using an intensified charge couple device (claim 35, in part),
- L) detecting using a near-field scanning microscope (claim 35, in part),
- M) detecting using a far-field confocal microscope (claim 35, in part),
- N) detecting using a microscope which detects wide-field epi-illumination (claim 35, in part),
- O) detecting using evanescent wave excitation (claim 35, in part),
- P) detecting using a total internal reflection fluorescence microscope (claim 35, in part),

Art Unit: 1637

Q) detecting using a method comprising a four color evanescent wave excitation device (claim 36),

R) detecting using fluorescence resonance energy transfer (claim 37, in part),

S) detecting using an electron transfer mechanism (claim 37, in part),

T) detecting using an excited-state lifetime mechanism (claim 37, in part),

U) detecting using ground-state quenching mechanism (claim 37, in part),

V) detecting measuring a residence time of labeled NTP in the complex (claim 38).

Species of residence time of NTP

W) residence time of an NTP that is incorporated into the primer nucleic acid is at least about 100 times longer to about 10,000 times longer than the residence time of an NTP that is not incorporated (claim 39),

X) residence time of an NTP that is incorporated into the primer nucleic acid is at least about 200 times longer to about 500 times longer than the residence time of an NTP that is not incorporated (claim 40),

Y) the residence time of an NTP that is incorporated into the primer nucleic acid is about 1.0 milliseconds to about 100 milliseconds (claim 41),

Z) the residence time of an NTP that is incorporated into the primer nucleic acid is about 2.0 milliseconds to about 10 milliseconds (claim 42).

Species of further steps of the method

AA) the step of genotyping said target nucleic acid by determining the identity of at least one NTP that is incorporated into a single molecule of the primer (claim 43),

AB) sequencing said target nucleic acid by determining the identity and sequence of incorporation of NTPS that are incorporated into a single molecule of the primer (claim 44).

The species are independent or distinct because in case of Group I, each of the species results in a different structure of the complex. In case of Group II, each of the species results in the method steps performed in a different way.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1 and 29 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. Upon election of one of the groups, Applicant is required to elect one species from each of the sets of species. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

8. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
7/8/06